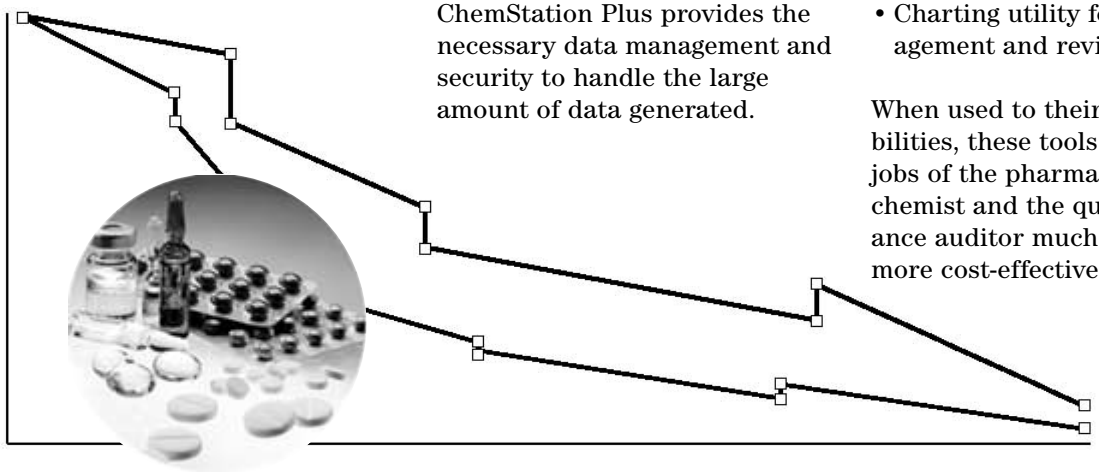
Using ChemStation Plus to Track Data from Drug Stability Studies

Application Note

Introduction

Drug stability is one of the most often studied characteristics in pharmaceutical testing. Large numbers of batches stored under different conditions are tested, resulting in large amounts of data that needs to be characterized, studied and maintained for the life of the batch record.



This data also falls under FDA regulations for GLP and must comply with the guidelines for electronics records (21 CFR Part 11.)

Since most pharmaceutical drug testing uses liquid chromatography as the analytical technique, the market-leading 1100 Series HPLC system from Agilent Technologies provides a perfect solution for testing, and Agilent ChemStation Plus provides the necessary data management and security to handle the large amount of data generated.

ChemStation Plus has many features that make it ideal for storage and tracking of stability test data.

- Compliant data storage in a secure Oracle® database
- Unlimited custom fields together with sample information
- Query tools for easy data retrieval
- Custom calculator for calculations and statistics without using an external spreadsheet
- Charting utility for study management and review

When used to their fullest capabilities, these tools can make the jobs of the pharmaceutical chemist and the quality assurance auditor much easier and more cost-effective.

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Setup

The custom fields provide the ability to manage and query stability data. To be able to retrieve stability data and create charts for review, information such as lot number, stability timepoint and storage conditions must be entered with the sample information. To set up these fields, study managers need only to create these custom fields with the correct attributes.

For example, the stability timepoint needs to be an integer to be able to chart the numbers over time, and the lot number needs to be a text field to be able to include numbers and letters in the lot designation. Since storage conditions are usually fixed, a selection list can be used so that users can choose from a list of preset conditions. This speeds up data entry and eliminates mistakes. Figures 1 through 4 show the setup screens for each of these fields.

Once set up in the system, these custom fields are available for use with studies. Studies are logical groups of data within the database. Custom fields can also have quality parameters associated with them. These fields can be set up as data entered manually, or as data entered programmatically by a ChemStation macro or function. The fields can also be made mandatory so that a user cannot make a run without entering data. Quality guidelines can be assigned such as maximum and minimum allowed values to help eliminate any errors on entry. Figure 5 shows the details of a custom field, including parameters for data entry.

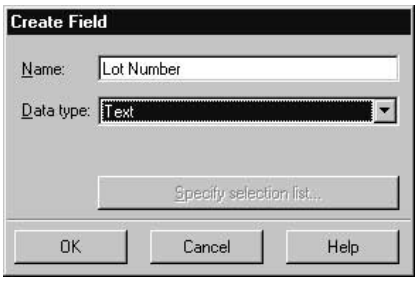


Figure 1
Creating a custom field for lot number

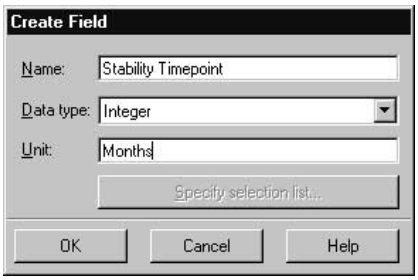


Figure 2
Creating a custom field for stability timepoint

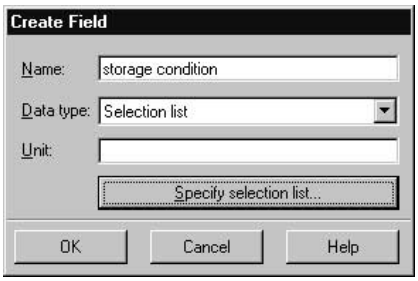


Figure 3
Creating a custom field for storage conditions

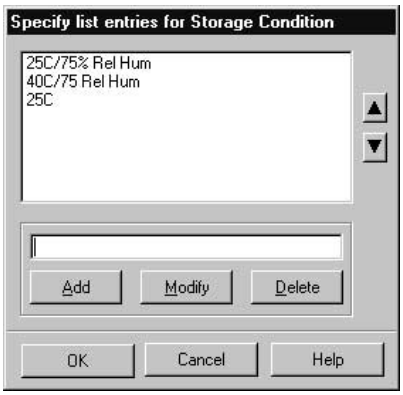


Figure 4
Specifying list entries for storage conditions

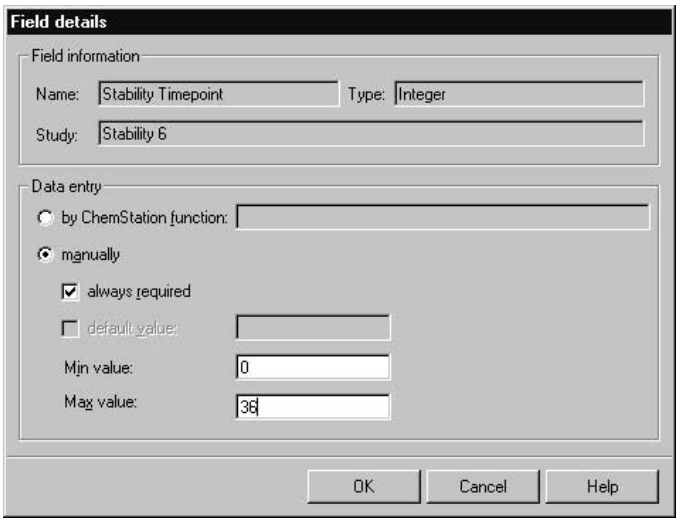


Figure 5
Custom field details, including type of data entry

When the custom fields have been set up, any user is now ready to run tests and use these extra features. During sequence setup, the user must fill in one more screen with these important data parameters. The ChemStore setup menu displays dialogs for the user to fill in an appropriate study name for the data and to set the custom fields. Figure 6 shows the sequence setup for the study using the three fields set up previously with the numeric stability timepoint, the picklist of storage conditions and the lot number of the drug substance.

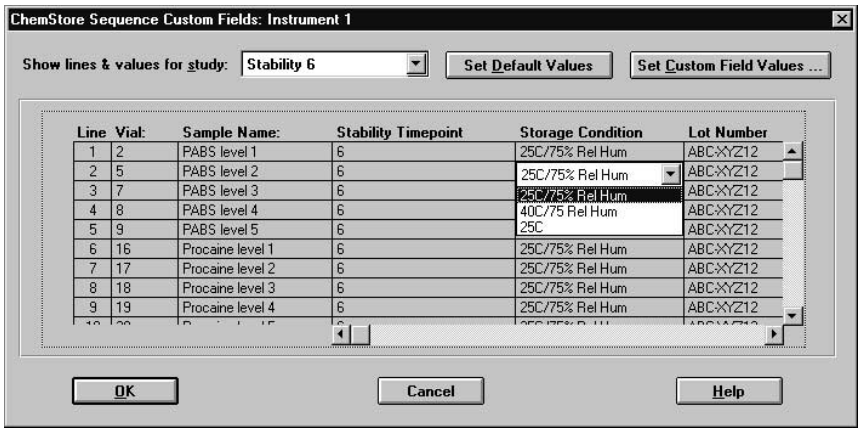


Figure 6
Setting up the sequence

During sequence execution, the following are transferred to the database after each run:

- method
- sequence
- all raw data
- all results that are calucated manually such as amounts, areas and retention times

The raw data also includes as fields:

- sample names
- method and sequence names
- timestamps
- user information
- level-4 information such as instrument name and serial number, column ID information (lot number, void volume, length, diameter and injection counts), error logs, and column performance data

All custom field information is available within the database and is linked to each sample that was run in the sequence.

Data Review

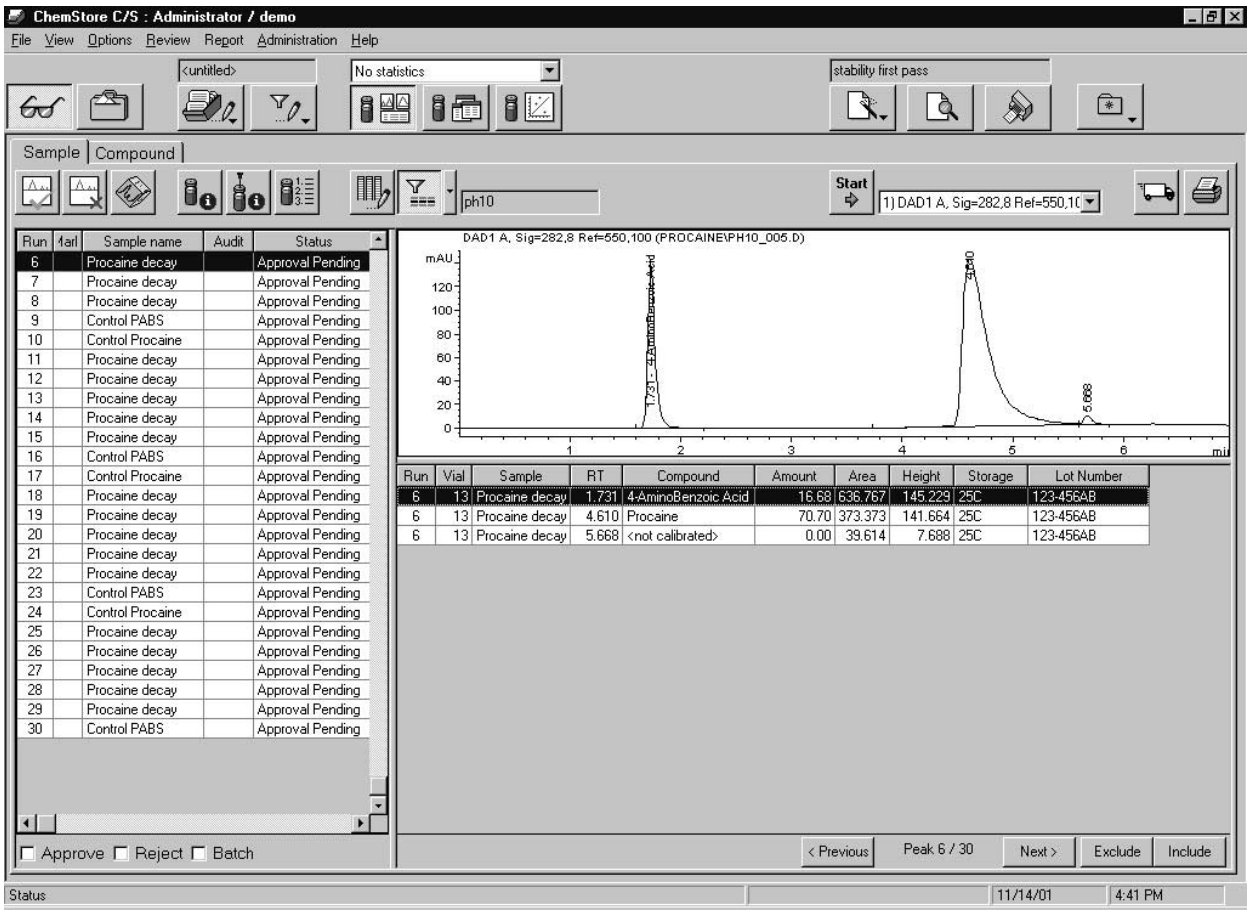
Because all the data is stored in the database, the user can now take advantage of the querying capabilities and gain a better understanding of the workings of the study, of the laboratory and of each individual timepoint of the study.

The database enables the user to run not only simple queries such as searching for each experiment across each sequence of data, but also complex, more meaningful queries, for example, searching for results of a single lot number across all instruments on which the experiments were performed.

Each query can search for exactly the data that is important to the reviewing person. First, all samples that fall within the parameters of the query are displayed in the review screen, see figure 7.

The samples are displayed as a list on the left side of the screen. The right side of the screen shows the results with chromatogram and spectra of the highlighted sample. The results can be any items from the database, which the user can choose using a simple table wizard. Additional filters allow the user to subdivide the query results further, for example, display only control samples in the query results. All data from the run and any custom fields are available as columns to make reviewing the data easy.

A possible query could be the reproducibility of %label claim in each timepoint charted in a control chart. The query would search for all samples of a particular lot that were run at a certain timepoint. Figure 7 shows a typical review screen, including the list of samples within the query specification, and the chromatogram and results of the highlighted sample. Another meaningful query would be to find out how each storage condition performed over the duration of the stability study.



Run	Vial	Sample	RT	Compound	Amount	Area	Height	Storage	Lot Number
6	13	Procaine decay	1.731	4-AminoBenzoic Acid	16.68	636.767	145.229	25C	123-456AB
6	13	Procaine decay	4.610	Procaine	70.70	373.373	141.664	25C	123-456AB
6	13	Procaine decay	5.668	<not calibrated>	0.00	39.614	7.688	25C	123-456AB

Figure 7
Review screen showing query results

This query would search for all samples with a particular lot number that were stored under certain storage condition.

The resulting set of data could then be summarized together with automatically calculated statistics, as shown in figure 8.

		Procaine			
Statistics	Run No.	Amount	RT	Area	Height
Count	14	14	14	14	14
Sum	105.00	7521.67	64.06	55888.30	3200.18
Minimum	1.00	526.58	4.51	3912.39	220.77
Maximum	14.00	541.64	4.61	4024.64	234.22
Mean	7.50	537.26	4.58	3992.02	228.58
Standard Deviation	4.1833	4.2510	0.0248	31.6767	4.7071
Rel. Std. Dev. (%)	55.7773	0.7912	0.5412	0.7935	2.0592
Variance	17.5000	18.0710	0.0006	1003.4113	22.1563

Figure 8
Table of statistical results

Charting

ChemStation Plus also has charting features allowing to create customized charts for better display of results. Any numerical results can be charted against others by simply selecting the x and y axes as shown in figure 9.

data item	X-axis	Y-axis
Run No.	☐	☐
Sample	☐	☐
Compound	☐	☐
Amount	☐	☑
RT	☐	☐
Area	☐	☐
Height	☐	☐
Stability Timepoint	☑	☐
Storage Condition	☐	☐

Figure 9
Selection of data for charting

A simple control chart would be a plot of amount recovered against run number. When preliminary planning must include data such as stability timepoint, more powerful queries can produce charts of amount recovered against stability timepoint with the recovery timeline for the whole stability study at each storage condition, see figures 11 and 12.

The ChemStation Plus software can automatically add warning limits and critical limits at 2σ and 3σ for true control charts, see figure 10.

This data can be reviewed and charted within the networked data system, and at the same time comply fully with FDA regulations such as GLP/GMP and 21 CFR Part 11.

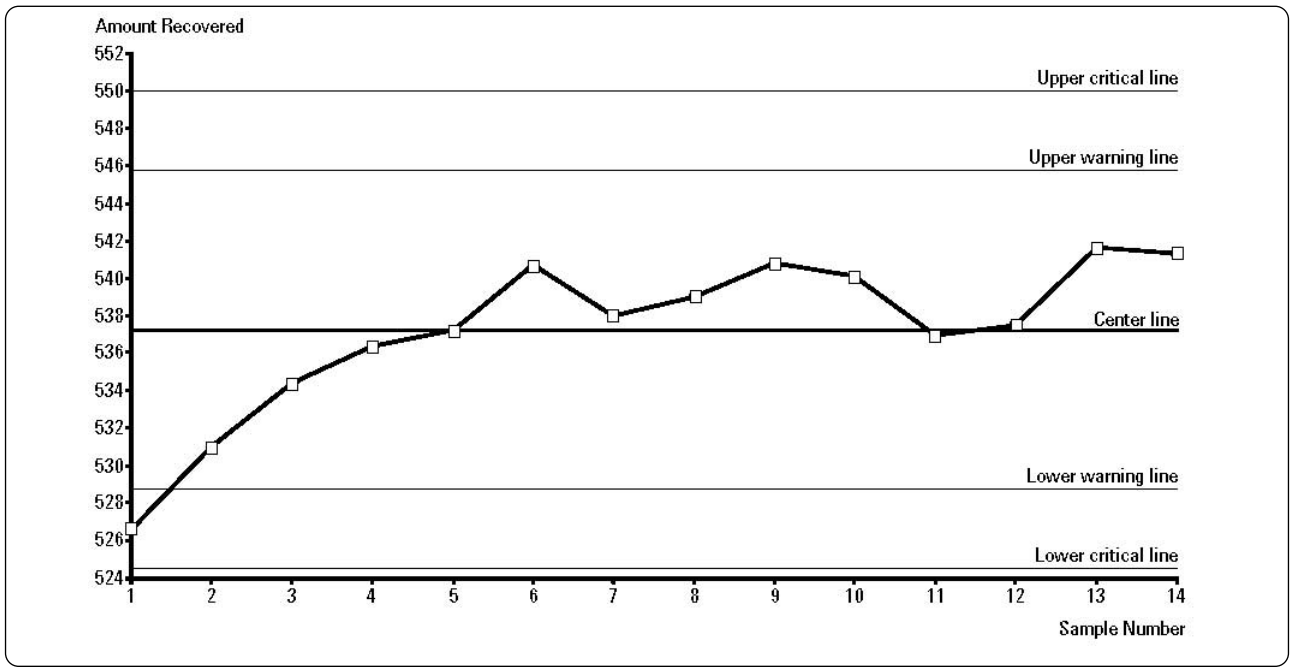


Figure 10
Reproducibility of amounts for the 6-month timepoint

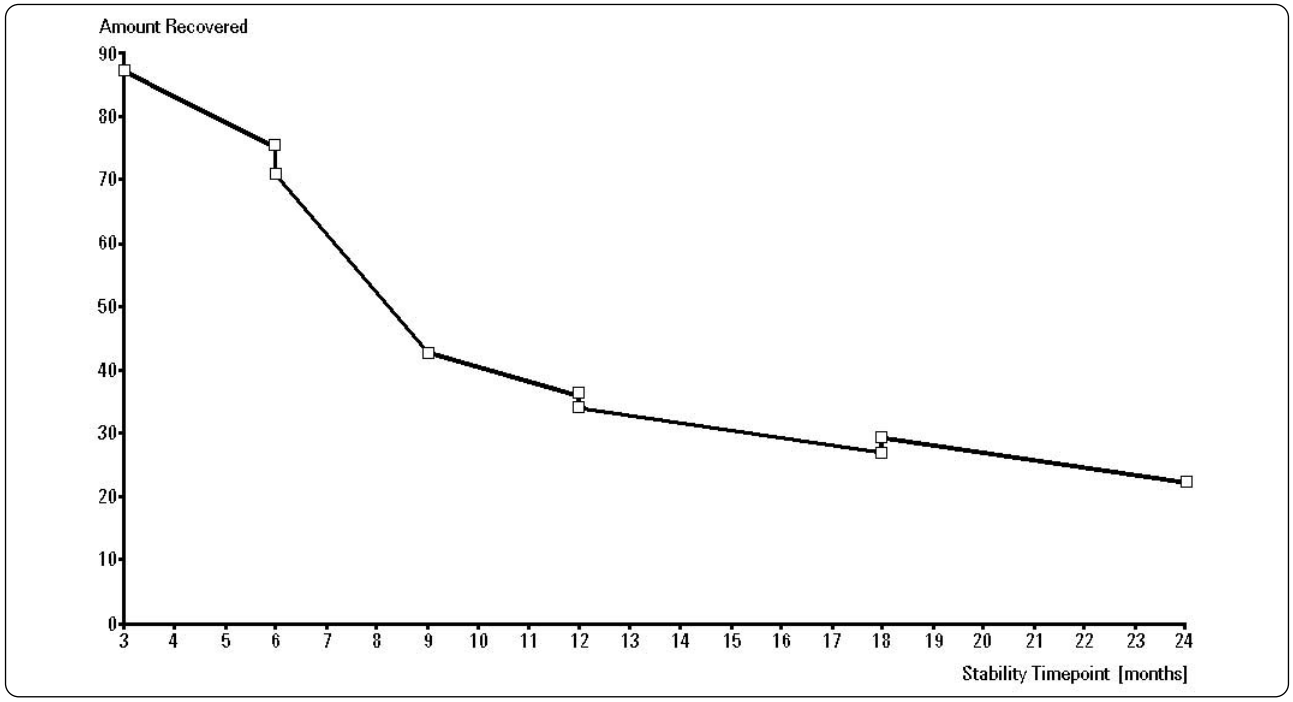


Figure 11
Stability study of drug at 25°C / 75% RH

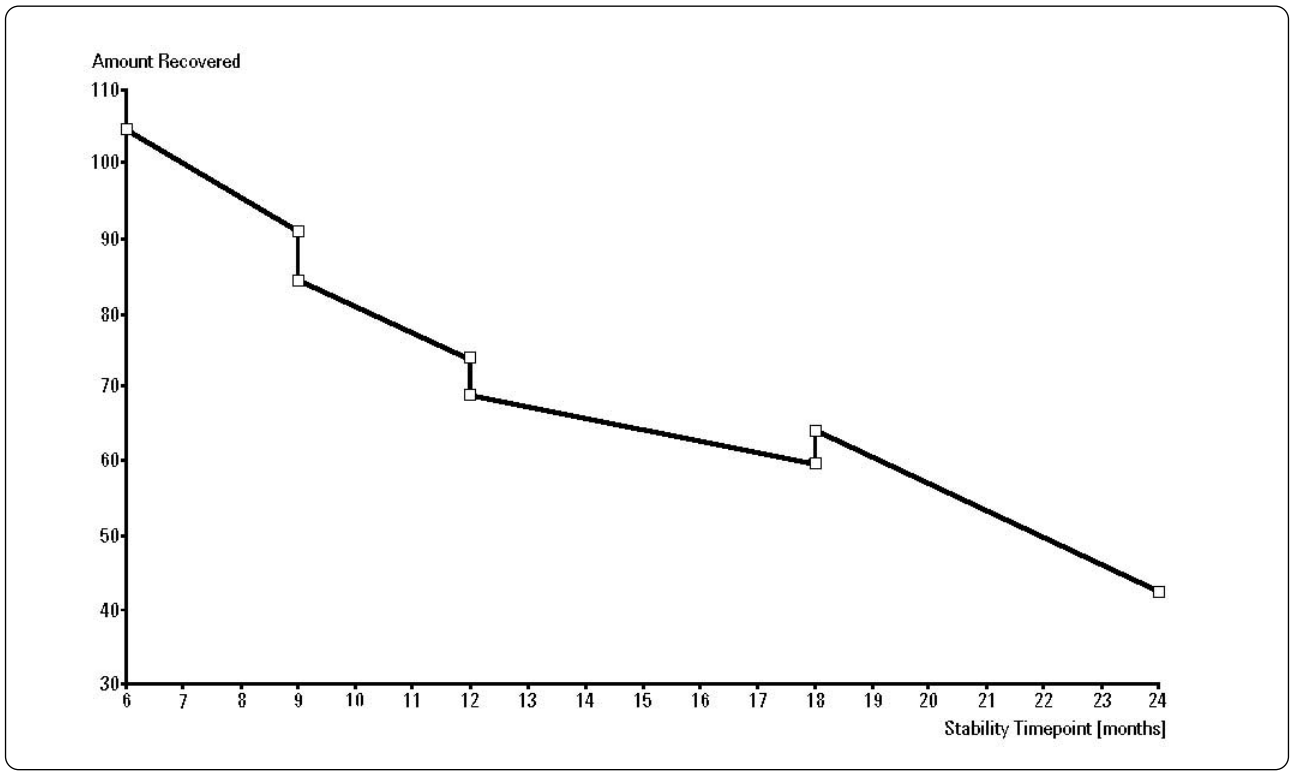


Figure 12
Stability study of drug at 25°C storage

All data can be summarized in tablular format with any particular columns chosen from the database, see figure 13. A simple table summarizing the results of multiple compounds can be easily created and saved as a specific user interface to review all data easily in the future. All this information can easily be exported with a single click to Microsoft® Excel, if more powerful data summarizing or calculations become necessary.

Sample					4-AminoBenzoic	Procaine
Run	Sample	Storage	Lot	Stability	Amount (Y)	Amount (Y)
2	Procaine	25C	123-456AB	3		86.88
2	Procaine	25C	123-456AB	3	6.72	
6	Procaine	25C	123-456AB	6		68.88
6	Procaine	25C	123-456AB	6	29.31	
8	Procaine	25C	123-456AB	9		58.50
8	Procaine	25C	123-456AB	9	37.04	
14	Procaine	25C	123-456AB	12		35.78
14	Procaine	25C	123-456AB	12	53.33	
17	Procaine	25C	123-456AB	18	60.53	
17	Procaine	25C	123-456AB	18		26.69
18	Procaine	25C	123-456AB	24		24.33
18	Procaine	25C	123-456AB	24	62.46	

Figure 13
Stability table

Summary

Stability studies have data sets that must be acquired over long periods of time and spread across multiple instruments and users. With its ability to acquire data from different analytical techniques and manage this data in compliance with FDA regulations, the ChemStation Plus networked data system provides a powerful tool to help the pharmaceutical chemist in the study of stability samples.

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